DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

February 11, 1997

Reference Number: 96-1048

Carl R. Illian, Ph.D.
Vice-President, Technical Affairs
Genetics Institute, Inc.
One Burtt Road
Andover, MA 01810

Dear Dr. Illian:

Enclosed is a biologics license issued in accordance with the provisions of section 351 of the Public Health Service Act. This license authorizes Genetics Institute to manufacture and ship for sale, barter or exchange in interstate and foreign commerce Coagulation Factor IX (Recombinant). Coagulation Factor IX (Recombinant) is indicated for the control and prevention of hemorrhagic episodes in patients with hemophilia B, including the peri-operative management of hemophilia B patients undergoing surgery.

Under this license you are authorized to manufacture Coagulation Factor IX (Recombinant) in nominal strengths of 250, 500 and 1000 I.U. per vial, under a contract manufacturing agreement with Sanofi Winthrop Pharmaceuticals. Change to the product, production process, equipment, facilities, or responsible personnel is required to be reported to FDA as specified in 21 CFR 314.70 and 601.12.

The dating period for this product shall be 24 months from the date of manufacture when stored at 2-8°C, during which period storage at room temperature not to exceed 25°C for up to 6 months is also permitted. The date of manufacture shall be defined as the date of the initial sterile filtration of the formulated bulk. Results of ongoing stability studies should be submitted throughout the dating period as they become available.

We acknowledge your commitment to continue the following clinical studies in order to fully characterize the thrombogenicity and immunogenicity of Coagulation Factor IX (Recombinant) and its safety profile in previously untreated patients:

C9408-21 Safety and Efficacy of Coagulation Factor IX (Recombinant) in Previously Treated Patients with Moderate or Severe Hemophilia B.
All patients currently enrolled in this study will continue in the study for a period of 2 years.

C9418-21 Study of the Safety and Efficacy of Coagulation Factor IX (Recombinant) in

Previously Untreated Patients with Severe or Moderate Hemophilia B
Approximately 30 patients with severe or moderately severe hemophilia B will be enrolled, at least 15 of whom will be severe hemophiliacs. All patients will be followed for at least 2 years and then up to 100 exposure days or 5 years, whichever is sooner.

All adverse experience reports should be submitted according to 21 CFR 600.80 to the Center for Biologics Evaluation and Research (CBER), HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, Maryland 20852-1448. In addition, safety related information obtained in the course of the ongoing clinical studies should be reported to BB-IND 5920 in accord with 21 CFR 312.32. It is also requested that distribution reports be submitted according to 21 CFR 600.81.

Coagulation Factor IX (Recombinant) manufactured by Genetics Institute is exempt from the lot release requirements of 21 CFR 610.2. However, we acknowledge your agreement to submit samples and release protocols for each lot of Coagulation Factor IX (Recombinant) released for distribution in the United States.

Please submit three (3) copies of final printed labeling at the time of use accompanied by Part II of FDA 2567 with completed implementation information. In addition, you may wish to submit your proposed introductory advertising and promotional campaign. If so, please submit three (3) copies of the proposed material in draft form with Part I of FDA Form 2567 to CBER, Advertising and Promotional Labeling Staff (APLS), HFM-202, 1401 Rockville Pike, Rockville, Maryland 20852-1448. Promotional claims should be consistent with and not contrary to the approved labeling. No comparative claims or claims of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the CBER. Final copies of advertising and promotional materials should be submitted at the time of use with Part II of FDA Form 2567 to APLS. Please include copies of the approved labeling with your proposed or final copy of advertising and promotional materials submitted to CBER.

Please acknowledge receipt of the enclosed license to the Director, Division of Application Review and Policy, HFM-585, 1401 Rockville Pike, Rockville, Maryland 20852-1448.

Sincerely yours,

Jay S. Epstein, M.D.
Director
Office of Blood Research and Review
Center for Biologics
Evaluation and Research